Response to Office Action dated 03/09/2010

Attorney Docket No.: 3535.022

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

- 1. (currently amended) A method for the *in vitro* differentiation between <u>non-septic</u> systemic inflammatory response syndrome systemic inflammatory non-infectious conditions (SIRS) and sepsis in a human subject systemic inflammatory infectious conditions (sepsis), comprising the following steps:
 - a. isolating sample RNA from a <u>blood sample from said human subject</u> <u>biological</u> <u>body fluid sample from a mammal suspected of having a systemic inflammatory</u> <u>non-infectious or systemic inflammatory infectious condition</u>;
 - b. marking at least one of
 - (i) the sample RNA and
 - (ii) at least one DNA, which has a gene activity that is specific for distinguishing between SIRS and sepsis and/or is a specific gene or gene fragment <u>having</u> at least 20 nucleotides,

with a detectable marker;

- c. bringing the sample RNA in contact with the DNA in hybridization conditions;
- d. bringing control RNA in contact with at least one DNA, under hybridization condition, said DNA representing a gene or gene fragment that is specific for distinguishing between SIRS and sepsis;
- e. quantitatively measuring the marking signals associated with the detectable marker of the hybridized sample RNA [[A]] and control RNA; and
- f. comparing the quantitative data of the marking signals; and
- g. in the case that genes or gene fragments that are specific for distinguishing between SIRS and sepsis are expressed more prominently or less prominently in the sample than in the control RNA, diagnosing the mammal as having SIRS or sepsis.

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2. (currently amended) The process according to <u>claim 33</u> <u>claim 1</u>, wherein prior to measurement of the sample-RNA the control-RNA is hybridized with the DNA and the <u>marker</u> signal associated with the detectable <u>marker</u> of the control-RNA/DNA-complex is

determined and is optionally recorded in the form of a calibration curve or table.

3. (previously presented) The process according to claim 2, wherein unchanged expression

level of gene from the sample and/or control-RNA was used as the reference gene for

quantification.

4. (currently amended) The process according to claim 33 claim 1, wherein mRNA was

used as the sample-RNA.

5. (currently amended) The process according to claim 33 claim 1, wherein the RNA is

provided in predetermined locations, in particular immobilized upon a carrier in the form

of a microarray.

6. (currently amended) The process according to claim 33 elaim 1, wherein the process is

employed for differential diagnostic early recognition, for control of the clinical

treatment, for individual risk assessment for patients for evaluation of the probability of

response to the specific treatment as well as for post-mortem diagnosis for distinguishing

between SIRS and sepsis.

7. (canceled)

8. (currently amended) The process according to claim 7, wherein cell samples are in

certain cases subject to lysis treatment in order to release cellular contents.

9. (canceled)

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10. (currently amended) The process according to claims 1, wherein for distinction between SIRS and sepsis, specific gene and/or gene fragments are selected from the group consisting of SEQ-ID No. 1 through SEQ-ID No. 91, as well as gene fragments thereof with at least 5-2000, preferably 20-200, more preferably 20-80 nucleotides.

- 11. (currently amended) The process according to <u>claim 33</u> elaim 1, wherein at least 2-100 cDNAs are employed.
- 12. (currently amended) The process according to <u>claim 33 elaim 1</u>, wherein at least 200 cDNAs are employed.
- 13. (currently amended) The process according to <u>claim 33</u> claim 1, wherein at least 200-500 cDNAs are employed.
- 14. (currently amended) The process according to <u>claim 33</u> <u>claim 1</u>, wherein at least 500-1000 cDNAs are employed.
- 15. (currently amended) The process according to <u>claim 33 elaim 1</u>, wherein at least 1000-2000 cDNAs are employed.
- 16. (currently amended) The process according to <u>claim 33 elaims 1 or 10</u>, wherein the gene or gene fragments and/or sequences derived from their RNA listed in claim 10 are replaced by synthetic analogs, aptamers as well as peptido-nucleic acids.
- 17. (previously presented) The process according to claim 16, wherein the synthetic analogs of the genes include 5-100, in particular approximately 70 base pairs.
- 18. (currently amended) The process according to <u>claim 33</u> claim 1, wherein the detectable markers are a radioactive marker, in particular ³²P, ¹⁴C, ¹²⁵I, ¹⁵⁵Ep, ³³P, or ³H.

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19. (currently amended) The process according to <u>claim 33 elaim 1</u>, wherein as the detectable markers a non-radioactive marker, in particular a color or fluorescence marker, an enzyme marker or an immuno marker and/or quantum dots or an electric measurable signal in particular potentiometric and/or conductivity and/or capacitance change upon hybridization, is employed.

- 20. (currently amended) The process according to <u>claim 33</u> <u>claim 1</u>, wherein the sample-RNA and the control-RNA <u>and/or enzymatic or chemical derivatives</u> carry the same carrier markers.
- 21. (currently amended) The process according to <u>claim 33</u> <u>claim 1</u>, wherein the sample-RNA and the control-RNA <u>and/or enzymatic or chemical derivatives</u> carry different markers.
- 22. (currently amended) The process according to <u>claim 33</u> claim 1, wherein the <u>immobilized or non-immobilized</u> samples carry a marker.
- 23. (currently amended) The process according to <u>claim 33 elaim 1</u>, wherein <u>a</u> the DNA sample is immobilized on glass or plastic.
- 24. (currently amended) The process according to <u>claim 33</u> claim 1, wherein the individual DNA molecules are immobilized by a covalent bonding to <u>a</u> the carrier material.
- 25. (currently amended) The process according to <u>claim 33</u> <u>claim 1</u>, wherein the individual DNA molecules are immobilized by electrostatic and/or dipol-dipol and/or hydrophobic interaction and/or hydrogen bridges to the carrier materials.
- 26. (canceled)
- 27. (canceled)

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- 28. (Canceled).
- 29. (Canceled).
- 30. (Canceled).
- 31. (Canceled).
- 32. (Canceled).
- 33. (new) A method for differentiating non-septic systemic inflammatory response syndrome (SIRS) from sepsis in a human subject, said method comprising:
 - a. measuring the abundance of a plurality of mRNAs in a blood sample from said human subject; and
 - b. comparing the abundance of the plurality of mRNAs in the blood sample from said human subject to the abundance of the plurality of mRNAs in blood samples from a control population of human subjects with non-septic SIRS;

wherein the plurality of mRNAs comprises:

- (i) mRNA, expressed from the MAGED1 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 1;
- (ii) mRNA, expressed from the H1F2 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 2;
- (iii) mRNA, expressed from the DEFA4 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 3;
- (iv) mRNA expressed from the SLC2A1 gene, comprising at least 20t contiguous nucleotides of SEQ ID NO: 4;
- (v) mRNA, expressed from the IHPK1 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 5;
- (vi) mRNA, expressed from the IGLL1 gene, comprising at least 20

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contiguous nucleotides of SEQ ID NO: 6;

- (vii) mRNA, expressed from the FLJ12085 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 7;
- (viii) mRNA, expressed from the CA1 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 9;
- (ix) mRNA, expressed from the ZAP70 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 10;
- (x) mRNA, expressed from the IGHM gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 78;
- (xi) mRNA, expressed from the KIAA0481 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 79;
- (xii) mRNA, expressed from the IGKV1D-12 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 81; and
- (xiii) mRNA, expressed from the KLF1 gene, comprising at least 20 contiguous nucleotides of SEQ ID NO: 87;

wherein an increased likelihood of the presence of sepsis in said human subject is determined when the abundance of the plurality of mRNAs in the blood sample from said human subject is statistically significantly greater than abundance of the plurality of mRNAs in blood samples from a control population of human subjects with non-septic SIRS.

- 34. (new) A method for differentiating non-septic systemic inflammatory response syndrome (SIRS) from sepsis in a human subject, comprising the following steps:
 - a. isolating sample RNA from a blood sample from the human subject;
 - b. marking at least one of
 - i. the sample RNA and
 - ii. at least one DNA, which has a gene activity that is specific for distinguishing between SIRS and sepsis and/or is a specific gene or gene fragment having at least 20 nucleotides,

with a detectable marker;

c. bringing the sample RNA in contact with the DNA in hybridization conditions;

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d. bringing control RNA in contact with at least one DNA, under hybridization condition, said DNA representing a gene or gene fragment that is specific for distinguishing between SIRS and sepsis;

- e. quantitatively measuring the signals associated with the detectable marker of the hybridized sample RNA and control RNA; and
- f. comparing the quantitative data of the signals associated with the detectable marker; and
- g. in the case that genes or gene fragments that are specific for distinguishing sepsis are expressed more prominently or less prominently in the sample than in the control RNA, diagnosing the mammal as having sepsis, wherein more prominent expression is characterized by the combination: mean Cy5vsCy3 of greater than 0.62 and Cy3vsCy5 of greater than 0.54, and wherein less predominant expression is characterized by the combination: mean Cy5vsCy3 of less than -0.21 and Cy3vsCy5 of less than -0.22.
- 35. (new) The process according to claims 34, wherein the diagnosis is based on a determination that at least 13 genes or gene fragments are expressed more prominently.
- 36. (new) The process according to claims 34, wherein the diagnosis is based on a determination that at least 17 genes or gene fragments are expressed less prominently.
- 37. (new) The process according to claims 34, wherein the diagnosis is based on a determination that one or more genes selected from SEQ:ID No. 1-10, 13, 15, 17-19, 21-24, 27-41, 43-45, 47-56, 78, 79, 81, 87 and 90 are expressed more prominently.
- 38. (new) The process according to claims 34, wherein the diagnosis is based on a determination that one or more genes selected from SEQ:ID No. 58, 61-74, 76 and 77 are expressed less prominently.